

JUL 12 2006

PTO/SB/21 (09-04)

Approved for use through 07/31/2006. OMB 0651-0031

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**TRANSMITTAL  
FORM**

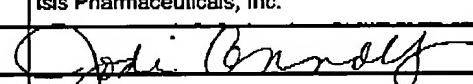
(to be used for all correspondence after initial filing)

|  |   |                        |                |
|--|---|------------------------|----------------|
|  |   | Application Number     | 10/561,324     |
|  |   | Filing Date            | 12/20/2004     |
|  |   | First Named Inventor   | Bryan Kraynack |
|  |   | Art Unit               | not assigned   |
|  |   | Examiner Name          | not assigned   |
| Total Number of Pages in This Submission | 3 | Attorney Docket Number | CHEM0021USA    |

**ENCLOSURES (Check all that apply)**

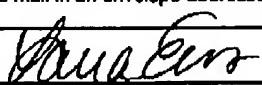
|  |   |   |
|--|---|---|
| <input type="checkbox"/> Fee Transmittal Form  | <input type="checkbox"/> Drawing(s)                                       | <input type="checkbox"/> After Allowance Communication to TC  |
| <input type="checkbox"/> Fee Attached  | <input type="checkbox"/> Licensing-related Papers                         | <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences                           |
| <input type="checkbox"/> Preliminary Amendment   | <input type="checkbox"/> Petition   | <input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief)                       |
| <input type="checkbox"/> Amendment/Reply   | <input type="checkbox"/> Petition to Convert to a Provisional Application | <input type="checkbox"/> Proprietary Information  |
| <input type="checkbox"/> After Final   | <input type="checkbox"/> Power of Attorney, Revocation                    | <input type="checkbox"/> Status Letter  |
| <input type="checkbox"/> Affidavits/declaration(s)   | <input checked="" type="checkbox"/> Change of Correspondence Address      | <input checked="" type="checkbox"/> Other Enclosure(s) (please identify below):<br>Start Under 37 CFR 3.73(b) |
| <input type="checkbox"/> Extension of Time Request   | <input type="checkbox"/> Terminal Disclaimer                              |   |
| <input type="checkbox"/> Express Abandonment Request   | <input type="checkbox"/> Request for Refund                               |   |
| <input type="checkbox"/> Information Disclosure Statement  | <input type="checkbox"/> CD, Number of CD(s) _____                        |   |
| <input type="checkbox"/> Certified Copy of Priority Document(s)                                    | <input type="checkbox"/> Landscape Table on CD                            |   |
| <input type="checkbox"/> Reply to Missing Parts/ Incomplete Application                            |   |   |
| <input type="checkbox"/> <input type="checkbox"/> Reply to Missing Parts under 37 CFR 1.52 or 1.53 |   |   |
| Remarks  |   |   |

**SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT**

|              |   |          |        |
|--------------|---|----------|--------|
| Firm Name    | Isis Pharmaceuticals, Inc.  |          |        |
| Signature    |  |          |        |
| Printed name | Jodi L. Connolly, Ph.D.   |          |        |
| Date         | 07/11/2006  | Reg. No. | 54,044 |

**CERTIFICATE OF TRANSMISSION/MAILING**

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below:

|                       |   |      |           |
|-----------------------|---|------|-----------|
| Signature             |  |      |           |
| Typed or printed name | Laura Eames   | Date | 7/12/2006 |

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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PTO/SB/82 (04-05)

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|  |                               |                |
|--|-------------------------------|----------------|
| <b>REVOCATION OF POWER OF ATTORNEY WITH NEW POWER OF ATTORNEY AND CHANGE OF CORRESPONDENCE ADDRESS</b> | <b>Application Number</b>     | 10/561,324     |
|  | <b>Filing Date</b>            | 12/20/2005     |
|  | <b>First Named Inventor</b>   | Bryan Kraynack |
|  | <b>Art Unit</b>               |                |
|  | <b>Examiner Name</b>          |                |
|  | <b>Attorney Docket Number</b> | CHEM0021USA    |

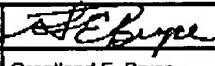
**I hereby revoke all previous powers of attorney given in the above-identified application.** A Power of Attorney is submitted herewith.**OR** I hereby appoint the practitioners associated with the Customer Number: 32,650 Please change the correspondence address for the above-identified application to: The address associated with Customer Number: 32,650**OR**

|  |       |     |  |
|--|-------|-----|--|
| <input type="checkbox"/> Firm or Individual Name |       |     |  |
| Address  |       |     |  |
| City   | State | Zip |  |
| Country  |       |     |  |
| Telephone  | Email |     |  |

I am the:

- Applicant/Inventor.  
 Assignee of record of the entire interest. See 37 CFR 3.71.  
*Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)*

**SIGNATURE of Applicant or Assignee of Record**

|           |   |           |              |
|-----------|---|-----------|--------------|
| Signature |  |           |              |
| Name      | Grantland E. Bryce  |           |              |
| Date      | 7/12/2006   | Telephone | 760-931-9200 |

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below.

 \*Total of \_\_\_\_\_ forms are submitted.

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JUL 12 2006

PTO/SB/98 (09-04)

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**STATEMENT UNDER 37 CFR 3.73(b)**Applicant/Patent Owner: Isis Pharmaceuticals, Inc.Application No./Patent No.: 10/561,324 Filed/Issue Date: 12/20/2005Entitled: **DOUBLE STRANDED COMPOSITIONS COMPRISING A 3'-ENDO MODIFIED STRAND FOR USE IN GENE MODULATION**

Isis Pharmaceuticals, Inc., a Corporation  
 (Name of Assignee) (Type of Assignee, e.g., corporation, partnership, university, government agency, etc.)

states that it is:

1.  the assignee of the entire right, title, and interest; or  
 2.  an assignee of less than the entire right, title and interest.  
 The extent (by percentage) of its ownership interest is \_\_\_\_\_ %

in the patent application/patent identified above by virtue of either:

A.  An assignment from the inventor(s) of the patent application/patent identified above. The assignment was recorded in the United States Patent and Trademark Office at Reel 17160, Frame 0778, or for which a copy thereof is attached.

OR

B.  A chain of title from the inventor(s), of the patent application/patent identified above, to the current assignee as shown below:

1. From: \_\_\_\_\_ To: \_\_\_\_\_  
 The document was recorded in the United States Patent and Trademark Office at  
 Reel \_\_\_\_\_, Frame \_\_\_\_\_, or for which a copy thereof is attached.
2. From: \_\_\_\_\_ To: \_\_\_\_\_  
 The document was recorded in the United States Patent and Trademark Office at  
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Additional documents in the chain of title are listed on a supplemental sheet.

Copies of assignments or other documents in the chain of title are attached.

[NOTE: A separate copy (i.e., a true copy of the original assignment document(s)) must be submitted to Assignment Division in accordance with 37 CFR Part 3, if the assignment is to be recorded in the records of the USPTO. See MPEP 302.08]

The undersigned (whose title is supplied below) is authorized to act on behalf of the assignee.

Grantland E. Bryce

Signature

7/12/2006

Date

Grantland E. Bryce

760-931-200

Printed or Typed Name

Telephone Number

Vice President, General and Legal Counsel

Title

This collection of information is required by 37 CFR 3.73(b). The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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